Hypertension

AHA SCIENTIFIC STATEMENT

Management of Stage 1 Hypertension in Adults With a Low 10-Year Risk for Cardiovascular Disease: Filling a Guidance Gap

A Scientific Statement From the American Heart Association

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ABSTRACT: High blood pressure (BP) is the leading cause of worldwide cardiovascular disease morbidity and mortality. Patients and clinicians dealing with hypertension have benefited from the evidence of event-based randomized controlled clinical trials. One result from those trials has been the development of evidence-based guidelines. The commitment to using evidence from these event-based randomized trials has been a cornerstone in the development of guideline treatment recommendations. However, in some situations, evidence from event-based trials is not available to guideline writers or clinicians for assistance in treatment decision making. Such is the case for the management of many patients with stage 1 hypertension. The purpose of this scientific statement is to provide information complementary to the 2017 Hypertension Clinical Practice Guidelines for the patient with untreated stage 1 hypertension (systolic BP/diastolic BP, 130–139/80–89 mm Hg) with a 10-year risk for atherosclerotic cardiovascular disease <10% who fails to meet the systolic BP/diastolic goal (<130/80 mm Hg) after 6 months of guideline-recommended lifestyle therapy. This statement provides evidence from sources other than event-based randomized controlled clinical trials and offers therapy options for consideration by clinicians.

Key Words: AHA Scientific Statements ■ heart disease risk factors ■ hypertension ■ pharmacotherapy

In recent decades, the management of cardiovascular disease (CVD) risk factors, including hypertension, has benefited from the evidence from event-based randomized controlled clinical trials (RCTs). One result from those trials has been the development of evidence-based guidelines.[1] The commitment to using evidence from these event-based randomized trials has been a cornerstone in the development of guideline treatment recommendations.[2] However, in some situations, evidence from event-based trials is not available to guideline writers or clinicians for assistance in treatment decision making. Such is the case for the management of many patients with stage 1 hypertension.[1,3]

The purpose of this scientific statement is to provide information complementary to the 2017 Hypertension Clinical Practice Guidelines for the patient with untreated stage 1 hypertension (systolic blood pressure [SBP]/diastolic BP [DBP], 130–139/80–89 mm Hg) and a 10-year risk for atherosclerotic CVD (ASCVD) <10% who fails to meet the SBP/DBP goal (<130/80 mm Hg) after 6 months of guideline-recommended lifestyle change. This statement provides evidence from sources other than event-based RCTs and offers therapy options for consideration by clinicians.[4]

High blood pressure (BP) is the leading cause of worldwide CVD morbidity and mortality. The global

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prevalence of SBP levels >110 mm Hg increased over the past 3 decades and was responsible for 10 million deaths and 212 million disability-adjusted life-years worldwide in 2015, representing a 1.4-fold increase since 1990.[5] Individuals with hypertension have higher lifetime risks for CVD and experience the onset of CVD morbidity 5 years earlier than individuals with normal BP.[6,7] Among middle-aged adults, every 20–mm Hg increase in SBP is associated with a doubling in the rate of death resulting from stroke, ischemic heart disease, and other vascular causes.[8] A recent analysis of adults in MESA (Multi-Ethnic Study of Atherosclerosis) who had an SBP between 90 and 129 mm Hg and were at low risk for ASCVD demonstrated a progressive stepwise increase in prevalent coronary calcium, traditional CVD risk factors, and incident CVD events with higher levels of SBP at baseline.[9] As indicated in an accompanying editorial, this study may identify the ideal SBP (90 mm Hg) to prevent the early stages of ASCVD.[10] Among American adults from 2011 to 2014, 42.3% had normal BP (SBP/DBP <120/80 mm Hg), 12.1% had elevated BP (120–129/<80 mm Hg), 13.7% had stage 1 hypertension (130–139/80–89 mm Hg), 7.7% had stage 2 hypertension (≥140/90 mm Hg), and 24.2% were taking antihypertensive medication.[11] Even among young adults in the CARDIA study (Coronary Artery Risk Development in Young Adults), a large proportion of participants in this biracial cohort had elevated BP (9%), stage 1 hypertension (25%), or stage 2 hypertension (13%) by 40 years of age.[12] It is increasingly clear that BP levels above those considered normal (≥120/80 mm Hg) in early adulthood are associated with higher long-term risk for CVD even if the individual's calculated 10-year risk is low. Not only is stage 1 hypertension common among young and middle-aged adults, but the majority of these individuals will progress to stage 2 hypertension, with an even higher risk of ASCVD. Among middle-aged adults (35–59 years of age) in China with stage 1 hypertension, 65% progressed to stage 2 hypertension within 15 years. In addition, >26% of all CVD deaths and 13% of all deaths were attributed to stage 1 hypertension.[13]

ADULT GUIDELINE RECOMMENDATIONS AND THE LACK OF RANDOMIZED TRIAL EVIDENCE

The 2017 Hypertension Clinical Practice Guidelines recommended lifestyle therapy for adults with stage 1 hypertension and a 10-year risk for CVD <10%. It is recommended that the BP measurement be repeated at 3- to 6-month intervals. For patients who fail to meet the <130/80–mm Hg treatment goal, no further guidance is offered.[1]

There is a lack of RCTs that have evaluated CVD outcomes among individuals with stage 1 hypertension and a low 10-year risk.[14] Because age is such a strong CVD risk factor, many of these patients are young adults. The long duration to the first CVD event and overall low CVD event rates for most young people would require trials with a large sample size or long time horizon to be adequately powered to detect differences in important clinical outcomes. Associated costs and logistical challenges make it unlikely that such trials will be conducted in the current research environment. This situation is similar in hypercholesterolemia in that there are early onset and progressive accrual of CVD risk among patients with hypercholesterolemia and a lack of large-scale outcome trials demonstrating treatment benefit in low-risk populations. As a result of these obstacles, the medical community must rely on findings from population studies, health services research, clinical trials with surrogate end points, and inferences from clinical trials performed in higher-risk groups for treatment guidance in this population.[15]

Costs have increased substantially as clinical trials in CVD have grown in size, scope, and complexity.[16] Novel statistical approaches have been proposed to increase power and to reduce sample size and cost. Furthermore, large pragmatic trials, randomized registry trials, and conduct of trials with target outcome damage or intermediate indicators of CVD end points all represent trial design features that may provide the opportunity to answer clinical questions that previously could not be answered.[17,18] These innovations may allow conduct of affordable RCTs that provide informative outcomes in young adults with a lower risk of ASCVD.

THE CONTRAST OF PEDIATRIC GUIDELINE RECOMMENDATIONS FOR ADOLESCENTS

The management of hypertension in adolescents recommended in the American Academy of Pediatrics 2017 "Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents" (AAP-CPG) is based on evidence of hypertension-associated target organ damage (TOD) in adolescents, as well as evidence that BP levels at a higher range in adolescence tend to increase progressively, leading to hypertension in early adulthood.[19] Therefore, AAP-CPG treatment goals for hypertension in adolescents are based on lowering the risk for TOD and reducing the risk for hypertension-related CVD in adulthood. For adolescents ≥13 years of age, the AAP-CPG definition of stage 1 hypertension is identical to that of the 2017 Hypertension Clinical Practice Guidelines. The optimal BP treatment goal for stage 1 hypertension in adolescents is SBP/DBP <90th percentile or <130/80 mm Hg, whichever is lower. The initial treatment recommended for stage 1 hypertension, in the absence of diabetes or chronic kidney disease, is nonpharmacological

lifestyle modification. This treatment approach includes providing counseling on controlling weight, consuming a healthy diet, increasing physical activity, and improving other modifiable risk factors, along with BP monitoring for up to 6 months. If there is no reduction in BP to goal after 6 months of lifestyle modification, pharmacological treatment is recommended. The AAP-CPG recommends obtaining an echocardiogram as a baseline measure when considering pharmacological treatment and provides detailed guidance on initial drug choices and drug titration to achieve the BP treatment goal.

Several reports that have applied the AAP-CPG definitions to pediatric populations identified a higher prevalence of pediatric hypertension and elevated BP compared with prior guidelines. Sharma et al[20] reported that children who were upclassified in BP category status with the use of the AAP-CPG criteria had other related risk factors for CVD, including obesity, elevated hemoglobin A_{1c}, and lipid abnormalities, thus identifying children with increased overall CVD risk. Another study that examined the AAP-CPG definitions of childhood BP categories in the Bogalusa cohort found that they improved the prediction of subsequent hypertension and left ventricular hypertrophy in young adulthood.[21] An analysis of BP data in adolescents 10 to 17 years of age in a community-based primary care population demonstrated that among those with persistently elevated BP, progression to hypertension occurred in 5.9% over a 2-year period.[22] More recently, Yang et al[23] reported a meta-analysis of 12 eligible cohort studies of elevated BP in children and adolescents and intermediate markers or hard outcomes in adulthood. In this study, elevated BP in childhood was defined as BP >90th percentile or ≥120/80 mm Hg. The investigators determined that elevated BP in childhood was associated with arterial stiffness in adulthood as measured by pulse wave velocity (odds ratio [OR], 1.83 [95% CI, 1.39–2.40]), carotid intima-media thickness (OR, 1.60 [95% CI, 1.29 – 2.00]), and left ventricular hypertrophy (OR, 1.40 [95% CI, 1.20–1.64]). Despite some limitations in these prospective studies, they provide persuasive evidence that, without interventions, hypertension or elevated BP in youth is a progressive disorder that leads to the development of intermediate markers of CVD.

EFFECTIVENESS AND CHALLENGE OF LIFESTYLE THERAPY

Lifestyle changes designed to achieve a healthier diet, reduce sodium intake, enhance potassium intake, increase physical activity, and maintain abstinence of or moderation in alcohol intake are a cornerstone of hypertension prevention and treatment.[1] TOHP (Trials of Hypertension Prevention) demonstrated the effectiveness of lifestyle therapy for BP lowering and prevention of hypertension. However, even under optimal conditions in which behavioral counseling is delivered by an experienced team, the desired outcomes are hard to achieve and maintain over time. Phase 2 of the TOHP provided intervention counseling for a minimum of 36 months of follow-up in 1787 adults 30 to 54 years of age with what would now be classified as stage 1 hypertension and a body mass index representing 110% to 165% of ideal body weight.[24] Baseline sodium intake (≈4200 mg/d) was reduced by 42%, 32%, and 27% at 6, 18, and 36 months in those randomly assigned to sodium reduction alone and by 36%, 25%, and 19% in those assigned to both sodium reduction and weight loss. For the corresponding follow-up visits, baseline weight (≈207 lb) was reduced by 4.7%, 2.1%, and 0.2% in those randomly assigned to weight loss alone and 4.3%, 2.3%, and 0.3% in those assigned to the combination of weight loss and sodium reduction. Although the results for both sodium reduction and weight loss were significantly better in the intervention compared with the usual care group, these findings underscore the difficulty of achieving and maintaining behavioral interventions aimed at lowering BP.

Similar findings are described in adults at high risk for CVD. For example, in a randomized controlled trial conducted in 5145 adults 45 to 75 years of age (mean, 59 years) with diabetes and a body mass index ≥25 kg/m^2 (mean weight, 223 lb), those randomly assigned to a weight loss behavioral intervention had a body weight that was ≈8%, 6%, and 2.6% less than their counterparts assigned to the control group after 12 months, after 2 years, and at the end of the study (median follow-up, 9.6 years).[25]

It is even more challenging to achieve widespread acceptance and implementation of behavior change interventions in clinical hypertension management. The BP-lowering effect of individual lifestyle changes such as sodium reduction alone tends to be less than what is achieved with medications. Better BP reduction requires the use of more complicated behavioral interventions aimed at ≥2 factors such as the combination of sodium reduction and weight loss.[26] Another concern is that lifestyle intervention studies, unlike medication studies, have generally been focused on change in BP and provide only indirect evidence of a reduction in CVD events or outcome experience.[1,24,27,28]

Following conduct of TOHP and other lifestyle intervention studies, a feeding study, the DASH trial (Dietary Approach to Stop Hypertension), further demonstrated the effect of diet on BP.[29] Participants were randomized to a diet rich in fruits and vegetables or a combination diet of fruits and vegetables with low-fat dairy products and reduced saturated fat and total fat (DASH diet) or a no-intervention control diet. Compared with participants assigned to the control diet, those assigned to the DASH diet experienced a statistically significant decrease in BP. The DASH diet was efficacious regardless of hypertension status or race/ethnicity. In a subsequent feeding

study that examined the effect of the DASH diet and reducing sodium intake, alone and in combination, each intervention lowered BP, with the greatest effect being seen for those assigned to both the DASH diet and a reduced intake of dietary sodium.[30] The BP-lowering effect was greater in those with hypertension compared with those without hypertension and in Black participants compared to all others. In a 3-arm behavioral intervention randomized controlled trial conducted in 810 adults with stage 1 and stage 2 hypertension, an intervention that targeted physical activity, weight loss, reduced sodium intake, and reduced alcohol consumption provided alone or in combination with the DASH diet reduced BP compared with advice only.[31] Addition of the DASH diet resulted in slightly lower BPs at 6 months (primary outcome)[27] and 18 months,[32] but the differences were not statistically significant.

Despite the previously mentioned challenges, achievement and maintenance of lifestyle change are fundamentally important in efforts to reduce BP-related CVD risk. Various combinations of an unhealthy diet leading to weight gain, excessive consumption of sodium, insufficient potassium intake, insufficient physical activity, and excessive alcohol consumption are the cause of high BP and hypertension in most adults, and lifestyle change is the core strategy for the prevention and treatment of hypertension.[1] The Chronic Care Model and other contemporary best-practice paradigms for the prevention and control of hypertension emphasize the value of a multilevel framework centered on an informed, activated patient capable of substantial self-management, with strong support from a proactive practice team, family and friends, and provider structures, as well as community support systems that are organized to facilitate success.[33,34] Lifestyle change, a key component of the Chronic Care Model, can be facilitated by designation of a champion who is knowledgeable in behavior change techniques; use of information technology for patient education, support, and monitoring of initial goal achievement and long-term adherence to the recommended health behavior changes; and creation of a supportive environment in the health care setting, the patient's home, and the community. At the national level, initiatives such as health messaging to promote a healthy lifestyle, policy proposals to improve food labeling and processing, and promotion of food products, school and other meal programs, physical activity, and health insurance highlighting of healthy lifestyles represent important adjuncts to care.

THE OTHER EVIDENCE

Lifetime Risk for CVD

Before publication of the 2017 Hypertension Clinical Practice Guidelines, observational studies showed graded relationships of systolic BP levels between 114 mm Hg and 140 mm Hg to the risk for future CVD events (coronary artery disease, heart failure, stroke, transient ischemic attacks), CVD and stroke mortality, and total mortality with excess event rates in the range of 20% to 50%.[7,8,35] Higher risk ratios were present for those with higher BP (130/80–140/90 mm Hg versus 120/80–130/80 mm Hg), CVD mortality compared with total mortality, and SBP compared with DBP.

Since publication of the 2017 Hypertension Clinical Practice Guidelines, 3 reports on young adults stratified cohorts according to the revised hypertension definitions and confirmed these relationships in large cohorts with diverse populations (Table). In the CARDIA study, Yano et al.[35] demonstrated that Black and White men and women with elevated BP or stage 1 hypertension had CVD event rates ≈70% higher than those with a normal BP. In South Korea, a study of 2.5 million adults 18 to 39 years of age at baseline who were followed up for 10 to 13 years identified an ≈25% higher CVD event rate for those with untreated stage 1 hypertension at baseline compared with those with a normal BP.[36] A recent study in China found similar results.[37] For all of these studies, recorded events generally occurred at ages <55 years.

Lifetime Risk for Progression to Hypertension

In the United States, the prevalence of hypertension increases with age, and 82% of adults ≥75 years of age had hypertension in 2011 to 2014.[11] BP in childhood is a strong predictor of BP levels in adulthood. For example, in the Bogalusa Heart Study, there was a strong correlation between BP among children and adolescents 5 to 14 years of age and BP levels measured 15 years later (r=0.36–0.50 for SBP and r=0.20–0.42 for DBP, varying according to age, race, and sex).[38]

Longitudinal studies in the United States have shown a high cumulative incidence of hypertension over the life course. When hypertension was defined as SBP ≥130 mm Hg, DBP ≥ 80 mm Hg, or antihypertensive medication use in the CARDIA study, the cumulative incidence of hypertension from 18 to 55 years of age was 76%, 76%, 55%, and 40% in Black men, Black women, White men, and White women, respectively.[39] Even among CARDIA study participants with SBP <110 mm Hg and DBP <70 mm Hg when they were 18 to 30 years of age, 64% of Black adults and 33% of White adults developed hypertension by 55 years of age. In MESA, which defined hypertension as SBP ≥140 mm Hg, DBP ≥90 mm Hg, or antihypertensive medication use, the estimated 40-year cumulative incidence of hypertension from 45 to 85 years of age was 93%, 92%, 86%, and 84% among Black, Hispanic, White, and Chinese participants, respectively.[40]

Previous studies suggest that the age-related increases in BP that occur in the United States may

Table. Summary of Adjusted Hazard Ratios for CVD, CHD, and Stroke in 3 Reports

2017 ACC/AHA BP Categories	Son et al[36]		Yano et al[35]	Wu et al[37]
	Men	Women		
CVD				
Normal BP	Reference value	Reference value	Reference value	Reference value
Elevated BP	1.07 (1.03–1.11)	1.13 (1.05–1.22)	1.67 (1.01–2.77)	0.8 (0.28–2.30)
Stage 1 hypertension	1.25 (1.21–1.28)	1.27 (1.21–1.34)	1.75 (1.22–2.53)	1.82 (1.12–2.94)
Stage 2 hypertension	1.76 (1.70–1.81)	1.85 (1.71–2.01)	3.49 (2.42–5.05)	3.54 (2.18–5.77)
CHD				
Normal BP	Reference value	Reference value	Reference value	Reference value
Elevated BP	1.05 (1.00–1.10)	1.04 (0.93–1.16)	1.95 (1.01–3.77)*	NA
Stage 1 hypertension	1.23 (1.19–1.27)	1.16 (1.08–1.25)	1.56 (0.94–2.59)*	NA
Stage 2 hypertension	1.68 (1.61–1.75)	1.46 (1.29–1.66)	2.80 (1.66–4.72)*	NA
Stroke				
Normal BP	Reference value	Reference value	Reference value	Reference value
Elevated BP	1.10 (1.03–1.17)	1.23 (1.12–1.36)	1.87 (0.73–4.79)*	0.80 (0.24–2.70)
Stage 1 hypertension	1.30 (1.25–1.36)	1.37 (1.29–1.46)	1.70 (0.86–3.34)*	1.79 (1.03–3.11)
Stage 2 hypertension	1.99 (1.90–2.09)	2.18 (1.97–2.41)	4.39 (2.32–8.31)*	3.21 (1.82–5.68)

ACC/AHA indicates American College of Cardiology/American Heart Association; BP, blood pressure; CHD, coronary heart disease; CVD, cardiovascular disease; and NA, not applicable.

not be inevitable. There was substantial heterogeneity in BP levels across sites in the INTERSALT study, an investigation conducted among 52 populations from 32 countries and 5 continents.[41] In 4 populations (Yanomomo and Xingu Indians of Brazil and rural populations in Kenya and Papua New Guinea), there was no increase in mean SBP or DBP from 20 to 59 years of age. Even in the United States, not all adults experience increases in BP as they grow older. In an analysis of CARDIA study data, 21% of participants were estimated to have a low stable BP trajectory, defined by low BP at baseline with a small to no increase in BP over 25 years of follow-up.[39] In this trajectory group, mean SBP increased from 101 to 104 mm Hg and mean DBP increased from 62 to 64 mm Hg over 25 years, with only 3% of participants initiating antihypertensive medication. In the CARDIA study data, healthy behaviors, including a lower body mass index and higher adherence to the DASH-style diet, were associated with a lower risk for hypertension over 30 years of follow-up.[39]

END ORGAN DAMAGE IN YOUNG, LOW-RISK PATIENTS

Data from prospective cohort studies beginning in childhood provide insights into the onset of CVD in early adulthood. In a trajectory analysis of data from 5 prospective cohort studies on measures of cardiovascular health, including BP, Allen et al[42] identified an association of declining cardiovascular health status with increased carotid intima-media thickness in early adulthood. Other reports indicate that the onset of hypertension in early adulthood confers substantial risk for TOD compared with hypertension onset at a later age. An earlier trajectory analysis on data from the CARDIA study cohort identified 5 distinct mid-BP ([SBP+DBP]/2) trajectories. Compared with the lowest trajectory, the 2 highest BP trajectory groups had greater ORs for the development of a coronary artery calcification score ≥100. The adjusted ORs for the 2 groups with higher baseline BP were 2.28 (95% CI, 1.24–4.18) and 3.70 (95% CI, 1.66–8.20), respectively. Findings were similar for isolated systolic BP trajectories.[43]

These recent publications based on longitudinal analyses in cohorts of young adults with stage 1 hypertension demonstrate a heightened risk for premature adverse CVD outcomes. Additional research is needed to develop risk scores appropriate for young adults that facilitate identification of those who have an elevated risk for premature adverse CVD outcomes even with stage 1 hypertension. Clinical trials are also needed to develop optimal treatment for stage 1 hypertension in young adults. Additional data for hazard ratios in young adults with elevated BP and stage 2 hypertension are given in the Table.[36–38]

BLUNTING THE PROGRESSION OF HYPERTENSION

As noted, a large body of evidence supports nonpharmacological interventions to prevent hypertension and to control BP. In addition to these interventions, several randomized trials have demonstrated that pharmacological therapy can prevent the progression of hypertension

in patients with prehypertension (terms in use at the time of the study).

In TROPHY (Trial of Preventing Hypertension), 772 adults with SBP of 130 to 139 mm Hg or DBP between 85 and 89 mm Hg were randomized to candesartan 16 mg daily or placebo and followed up for the development of hypertension, defined by a mean SBP ≥140 mm Hg or DBP ≥90 mm Hg across 3 visits, or SBP ≥ 160 mm Hg or DBP ≥100 mm Hg during at least 1 follow-up visit, TOD, or other reasons to initiate pharmacological treatment.[44] Over 2 years, 13.6% and 40.4% of those randomized to candesartan and placebo, respectively, developed hypertension. Candesartan treatment was discontinued after 2 years, and participants were followed up for another 2 years for hypertension. Over the entire 4-year follow-up period, a smaller proportion of participants randomized to candesartan for 2 years developed hypertension compared with those randomized to placebo (53.2% versus 63.0%). According to this study, it was estimated that 4 people would require pharmacological treatment for 2 years to prevent 1 new case of hypertension. One important understanding from this trial was the need to continue antihypertensive therapy in order to prevent the occurrence of hypertension long term.

At least 2 other RCTs have demonstrated that pharmacological therapy can reduce the risk for hypertension. In the PREVER-Prevention trial (Prevention of Hypertension in Patients With Prehypertension), adults with SBP between 120 and 139 mm Hg or DBP between 80 and 89 mm Hg after 3 months of lifestyle change intervention, levels consistent with elevated BP and stage 1 hypertension in the 2017 Hypertension Clinical Practice Guidelines, were randomized to chlorthalidone/amiloride or placebo.[45] In this study, the cumulative incidence of hypertension, defined by a mean SBP ≥140 mm Hg or mean DBP ≥90 mm Hg across 2 visits, was 11.7% among participants in the chlorthalidone/amiloride arm versus 19.5% in those randomized to placebo. In addition, the intervention arm experienced reductions in electrocardiographic measures of left ventricular mass, supporting the concept that antihypertensive drug therapy averts subclinical pathophysiologic response to elevated BP and stage 1 hypertension. In the PHARAO study (Prevention of Hypertension With the ACE-Inhibitor Ramipril in Patients With High-Normal BP), patients with SBP between 130 and 139 mm Hg or DBP between 85 and 89 mm Hg were randomized to ramipril or placebo.[46] Over 3 years, 30.7% of those randomized to ramipril versus 42.9% of those randomized to placebo developed hypertension, defined by a mean SBP ≥140 mm Hg or mean DBP ≥90 mm Hg. In a trial of adults 18 to 36 years of age with DBP <85 mm Hg whose parents both had hypertension, SBP and DBP on ambulatory BP monitoring were lower after 1 year among participants randomized to candesartan 8 mg (−3.9 and −3.4 mm Hg for SBP and DBP, respectively), whereas there was no evidence of a change for participants randomized to placebo (0.3 and 0.6 mm Hg for SBP and DBP, respectively).[47] The proportion of participants who developed hypertension was not reported. These RCTs indicate that pharmacological treatment can be effective in lowering BP in stage 1 hypertension and in preventing progression to increasing BP levels.

SUGGESTIONS FOR FUTURE RESEARCH

Conducting an RCT in young adults with hard CVD events (death, nonfatal myocardial infarction, and stroke) would be difficult given the relatively low incidence of these outcomes in adults <40 years of age. Such a trial would require a very large sample size and longer than the usual 5 years of follow-up.

Alternative trial designs should be considered. Primary outcomes could be BP related, such as progression to stage 2 hypertension, cumulative exposure to BP, or intermediate markers of CVD or progression to TOD.

New trials could build on the designs used in TROPHY, PHARAO, and PREVER-Prevention by powering them to evaluate additional cardiac outcomes such as echocardiographic markers of left ventricular mass and cardiac function, incidence/progression of coronary artery calcium and vascular end points such as age-related increases in pulse wave velocity and carotid intima-media thickness, or reductions in ankle-brachial index. Ambulatory BP monitoring and home BP monitoring could also be included as outcome measurements.

The generalizability of prior trials to younger adults has been questioned, primarily because of their low risk for CVD. It is not possible or practical to repeat large randomized trials in every unstudied group. External generalizability should be considered in the design of new trials, and enrollment criteria should ensure that a diverse population is enrolled, with the capacity to assess outcomes across the age range of 20 to 50 years, and should include major racial and ethnic subgroups as well as women, including those with a history of hypertension during pregnancy.

Information technology and social media are the preferred forms of communication for young adults. Information technology may also improve monitoring of BP and other variables of interest. Incorporation of pharmacists, nurse practitioners, registered nurses, and community health workers into care plans may improve education and adherence. Other potential strategies include the use of a pragmatically structured national network in which eligible patients can be enrolled in clinical trials and followed up by application of cloud

technology and quality control algorithms that facilitate uploading and tracking of study data.[48,49] Finding incentives for practices to join such a network and for patients to participate with a high level of adherence to protocol requirements could potentially be accomplished by an amalgam of patient-centered outcome investigators, outcome measurement specialists, pragmatic trialists, and stakeholders (primary care providers and patients), all of whom currently exist.

CONSIDERATIONS FOR CLINICAL PRACTICE

As recommended in the 2017 Hypertension Clinical Practice Guidelines, patients with stage 1 hypertension who have an estimated 10-year ASCVD risk <10% should be managed with nonpharmacological (lifestyle) therapy and have a repeat BP evaluation within 3 to 6 months.[1] Patients should be informed that many individuals can achieve goal BP without the use of medication through vigorous implementation of lifestyle change therapy.

In all patients with stage 1 hypertension not achieving goal BP (<130/80 mm Hg) within 6 months, lifestyle therapy should be continued and consideration given to the addition of medication from among the 4 classes recommended in the 2017 guideline.[1]

For patients who were identified as having hypertension during adolescence (or childhood) and were prescribed antihypertensive drug therapy, consideration should be given to the original indications for starting drug treatment and the need to continue antihypertensive medication and lifestyle therapy as young adults.[50]

In young adults with stage 1 hypertension who are not controlled with lifestyle therapy, special consideration should be given to use of antihypertensive medication in individuals with a family history of premature CVD,[51] a history of hypertension during pregnancy,[52] or a personal history of premature birth.[53]

Careful attention to adherence issues should be given to young adults with stage 1 hypertension. Recommendations for adherence strategies to improve hypertension treatment and control are available in the 2017 Hypertension Clinical Practice Guidelines.[1] In busy practice settings with limited provider time and lack of expertise in behavior change techniques, lifestyle counseling by a trained/certified team member or nonpractice counselor is highly desirable.

As recommended in the 2019 American College of Cardiology/American Heart Association guidelines on the primary prevention of CVD, 10-year risk should be assessed every 4 to 6 years in patients with a 10-year risk <10%.[54]

As noted, the evidence for these considerations is based primarily on observational data. In the absence of randomized controlled trial data and with the lack of a plan for such studies to be performed, clinicians may use their clinical judgment in considering the option of medication for these patients.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on January 11, 2021, and the American Heart Association Executive Committee on February 22, 2021. A copy of the document is available at https://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com.

The American Heart Association requests that this document be cited as follows: Jones DW, Whelton PK, Allen N, Clark D 3rd, Gidding SS, Muntner P, Nesbitt S, Mitchell NS, Townsend R, Falkner B; on behalf of the American Heart Association Council on Hypertension; Council on the Kidney in Cardiovascular Disease; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Lifelong Congenital Heart Disease and Heart Health in the Young; and Stroke Council. Management of stage 1 hypertension in adults with a low 10-year risk for cardiovascular disease: filling a guidance gap: a scientific statement from the American Heart Association. *Hypertension*. 2021;77:e58–e67. doi: 10.1161/HYP.0000000000000195.

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Disclosures

Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Robert M. Carey	University of Virginia Health System	None	None	None	None	None	None	None
Daniel T. Lackland	Medical University of South Carolina	None	None	None	None	None	None	None
Jackson T. Wright Jr.	Case Western Reserve University	NHLBI (SPRINT Steering Committee)†; Ohio Department of Medicaid (HTN-QIP/CARDI-OH)†; NIDDK (CRIC Study)*	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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